A Break in Bruch's

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Introduction:

A 48-year-old Armenian male presented with 3-4 days of blurry vision in his left eye. He stated things had progressively worsened and he felt that his central vision was "wavy." He endorsed a prior ocular history significant for myopia, and central serous retinopathy in the right eye that was previously treated with photodynamic therapy (PDT). He denied taking any medications other than a daily multivitamin and denied any significant past medical or surgical history. Further his family history was significant only for cataracts in his mother and father. Systemically he was feeling well and denied any recent health changes. He also denied any skin changes or history of GI bleeding.

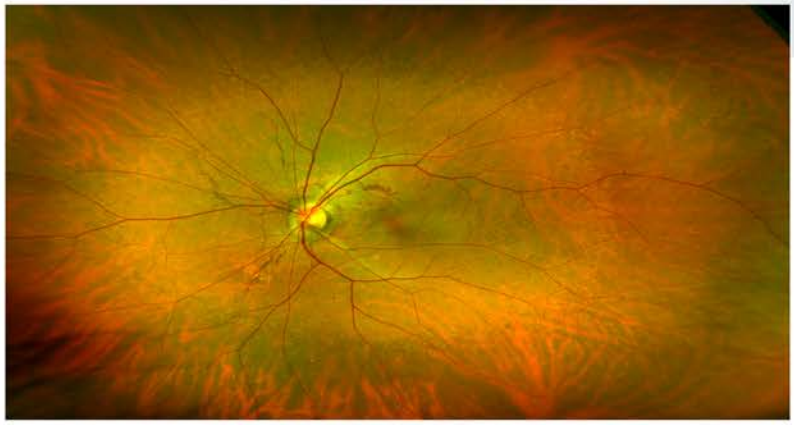

Figure 1 *(top): A widefield photo of the right eye demonstrating radiating streaks of peripapillary pigment mottling as well as granular pigmentation in the macula. Mid-peripheral granular pigmentation is also present.*

Figure 2 *(bottom): A widefield photo of the left eye demonstrating radiating streaks of peripapillary pigment mottling as well as granular pigmentation in the macula and an intraretinal hemorrhage in the superotemporal left macula. Mid-peripheral granular pigmentation is also present.*

Exam:

Visual acuity testing with correction was 20/20 in both eyes. Intraocular pressures were normal. Pupils were equal, round and reactive to light without evidence of a relative afferent pupillary defect. Confrontation visual fields were full. Slit lamp examination revealed an unremarkable anterior segment. The posterior segment demonstrated radiating streaks of peripapillary pigment mottling in both eyes as well as granular pigmentation in the right macula and an intraretinal hemorrhage in the superotemporal left macula. Granular pigmentary changes in the retinal mid-periphery in both eyes (Figures 1 and 2). Optical coherence tomography (OCT) demonstrated nasal granularity in both eyes corresponding to the peripapillary streaks seen on exam (Figure 3). Superior OCT cuts of the left macula revealed subretinal hyperreflective material and subretinal fluid, which corresponded to the area of intraretinal hemorrhage seen on exam (Figure 4). OCT-Angiography of the left eye confirmed the presence of a choroidal neovascular membrane (CNVM) (Figure 5). Fundus autofluorescence showed hyperautoflouesence over the area of the CNVM (Figure 6). Given these findings the differential diagnosis included angioid streaks, lacquer cracks, choroidal rupture, ocular histoplasmosis, and central serous retinopathy. His history, exam, and lack of prior ocular trauma suggested that the most likely diagnosis was angioid streaks. His blurry vision was caused by a new CNVM creating an area of retinal hemorrhage. Treatment with anti-VEGF therapy was recommended and an intravitreal injection of bevacizumab was given to the left eye. The patient experienced improvement in symptoms following treatment.

Work-Up:

The patient had previously been evaluated by his

primary care provider (PCP) for possible systemic associations with angioid streaks. In particular, he was evaluated for pseudoxanthoma elasticum (PXE). Additionally, a CBC and hemoglobin electrophoresis were completed and returned within normal limits. Overall, his prior systemic work-up with his PCP returned negative for any systemic correlation. Therefore, his angioid streaks were deemed to be idiopathic in nature.

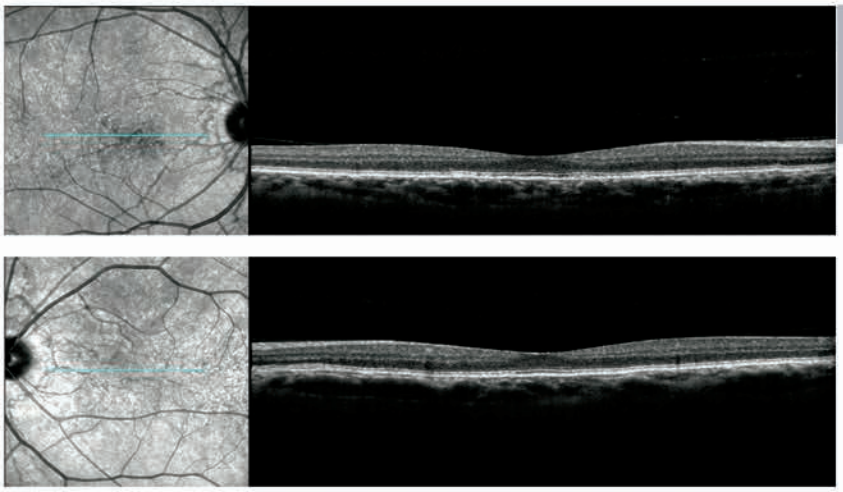

Figure 3: *OCT of the right (top) and left (bottom) eyes demonstrating nasal granularity.*

Discussion:

Angioid streaks tend to present as irregular, narrow lines that present bilaterally. These lines will radiate from the optic disc. The appearance of the streaks are due to crack-like dehiscences of calcified Bruch's membrane, thought to develop from the mechanical stress exerted by extraocular muscles on the posterior pole. It is this weakening of Bruch's membrane that predisposes these patients to the development of CNVMs when a rupture in Bruch's occurs. Angioid streaks were first described by Doyne in 1889 as irregular lines that extended from the disc margins. They were later renamed by Knapp in 1892 to angioid streaks as there was a belief that the disease process involved the vasculature. It is proposed that over 50% of patients with angioid streaks have a concurrent systemic disease. It is important to be aware of the multiple unique systemic associations that are commonly seen in patients with angioid streaks. There are multiple mnemonics that exist to aid in remembering the most common association, however the one that is most commonly used is PEPSI. The letters help one recall these important associations and are as follows: Pseudoxanthoma elasticum, Ehlers Danlos Syndrome, Paget's disease, Sickle Cell, and Idiopathic. It should be mentioned that Ehlers-Danlos is no longer believed to be highly correlated with Angioid Streaks as there are minimal case reports of this in the literature.

Of all the systemic associations, the most important one to be aware of is PXE as it has the highest association with angioid streaks. The incidence has been reported to be between 59-87%. Due to the fact that this disease damages the elastic fibers in the skin, cardiovascular system and retina, PXE can cause severe systemic issues in addition to the eye findings. The easily identifiable findings include skin changes of increased laxity with small yellow papular lesions that tend to develop on the neck, axillae, groin, and flexural creases. Additional systemic findings are GI bleeding, premature atherosclerosis, calcification of the blood vessels, and cerebral ischemia. Due to the risk of systemic morbidity and mortality this association is important to be aware of. When a work up is conducted on a patient with angioid streak one can consider coordinating with a patient's PCP for a skin biopsy to rule out PXE as well as a CBC and hemoglobin electrophoresis to rule out sickle cell anemia. Calcium and phosphate levels can be an additional study that can be useful when looking for Paget's disease.

Diagnosis of angioid streaks is largely clinical given the characteristic appearance. Additional imaging studies can be useful when the diagnosis is in question. Fluorescein angiography (FA) will demonstrate hyperfluorescence of the streaks due to overlying retinal pigment epithelial atrophy. OCT can identify calcification at the level of Bruch's membrane

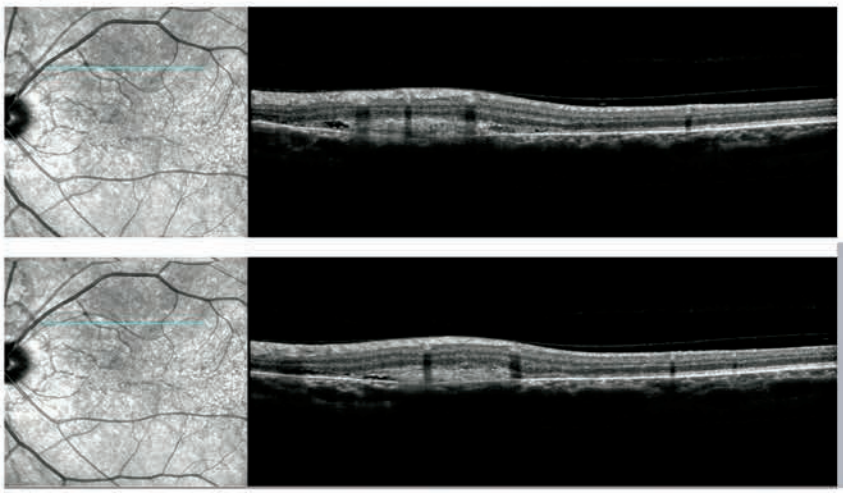

Figure 4: *OCT of the left eye showing subretinal hyperreflective material (SRHRM) and subretinal fluid corresponding to the area of hemorrhage seen in the color images.*

and may demonstrate subretinal fluid or subretinal hyperreflective material which can be seen when a CNVM has developed. In cases when FA is not readily available, OCT-A can also be quite useful as seen in our case. OCT-A will highlight the abnormal blood vessel network and help with localization.

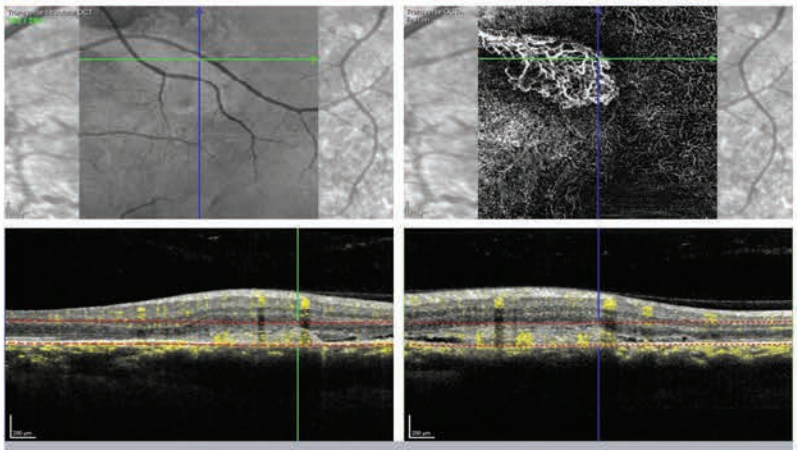

Figure 5: *OCT-Angiography demonstrating a choroidal neovascular membrane in the left eye.*

In patients that do go on to develop a CNVM, treatment with anti-VEGF agents are quite effective. Laser photocoagulation and PDT have also been investigated as another form of treatment, but have proven to be less successful. Currently, anti-VEGF treatment is the most effective treatment option for CNVM development in angioid streaks as the lesions tend to be highly responsive. Depending on the location of the lesion and size of the hemorrhage the visual prognosis can be favorable for patients.

Key Points:

- Angioid streaks is a diagnosis that has numerous systemic associations, which can be remembered with the mnemonic PEPSI
  - **P**seudoxanthoma elasticum (PEX)
  - **E**hlers Danlos (although no longer believed to be commonly associated with Angioid Streaks) the E is now from Pseudoxanthoma Elasticum
  - **P**aget's Disease
  - **S**ickle Cell Anemia
  - **I**diopathic
- CNVM formation can happen from ruptures in Bruch's membrane
- OCT and OCT-A can be helpful in confirming the presence of a CNVM
- CNVM from angioid streaks tend to be very responsive to anti-VEGF therapy, which is the current preferred treatment method.

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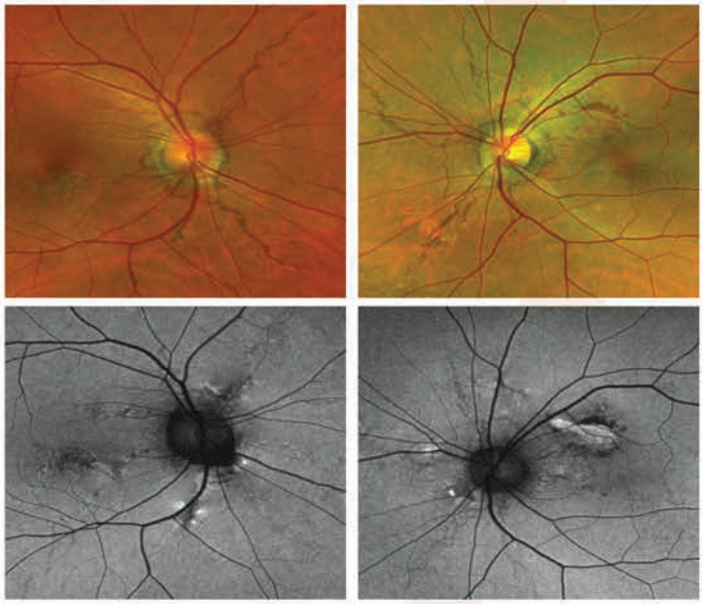

Figure 6: *Scanning images of the right and left eyes (top) demonstrating a magnified image of the peripapillary region with an intraretinal hemorrhage in the left eye. Fundus autofluorescence images of the right and left eyes (bottom) show hyperautofluorescence of the area corresponding to the CNVM and hypoautoflouresence representing the hemorrhage in the left eye.*

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